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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,251	02/27/2004	Darrell C. Conklin	97-72C5	9909

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Shelby J. Walker
Patent Department
ZymoGenetics, Inc.
1201 Eastlake Avenue East
Seattle, WA 98102

EXAMINER	
MERTZ, PREMA MARIA	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,251	CONKLIN ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 12/12/05

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *10-18,22-31,35,36,38-40,44,45 and 47-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,19-21,32-34,37,41-43 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/27/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 1-9, 19-21, 32-34, 37, 41-43, 46) in the reply filed on 12/12/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-9, 19-21, 32-34, 37, 41-43, 46 will be examined in the instant application.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title be amended to recite "polynucleotide encoding mammalian cytokine-like polypeptide-10".

Claim rejections-35 U.S.C. 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-9, 19-21, 32-34, 37, 41-43, 46 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to an expression vector comprising a DNA encoding a cytokine-like polypeptide-10 (interleukin-20, Zcyto10) 176 amino acids in length. The invention encompassed by this claim has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published on 1/5/01, 66 FR 1092. The instant

application has provided a description of an isolated protein, but does not disclose a specific and substantial biological role of this protein or its significance. There is no biological activity, phenotype, disease or condition, or any other specific feature that is disclosed as being associated with the IL-20 polypeptide. The mere identification of the polypeptide is not sufficient to impart any particular utility to the claimed polynucleotide without any information as to the specific properties of IL-20. Since significant further research would be required of a person skilled in the art to determine how the claimed expression vector encoding the IL-20 polypeptide is involved in any activities, the asserted utilities are not substantial.

Furthermore, since the asserted utility is not present in a ready-to-use, real-world application, the asserted utility is not substantial.

The specification asserts several utilities for the polypeptide of SEQ ID NO:2, that are not necessarily related to its biological activities; however, none of these asserted utilities meets the three-pronged test of being credible, specific and substantial. Each will be addressed in turn:

1. *to produce variant polypeptides*. This asserted utility is not specific or substantial. Since the same assays can be performed with any polypeptide, the asserted utility is not specific to the claimed polynucleotide encoding the polypeptide (SEQ ID NO:2). Also, since the specification does not disclose how the variants of the polypeptide, such as molecules with 50%, 60% and 80% homology to SEQ ID NO:2, can be used, significant further research would be required of a person skilled in the art to determine how to use the claimed variants. Since the asserted utility is not present in a ready-to-use, real-world application, the asserted utility is not substantial.

2. *to produce antibodies against the polypeptides*. This asserted utility is not specific or substantial. Since antibodies can be made to any polypeptide, the asserted utility is not specific to the IL-20 polypeptide. Furthermore, the specification does not disclose how anti-IL-20 antibodies can be used, and therefore further significant research would be required on one skilled in the art to determine how to use the claimed antibodies. Since the asserted utility is not presented in a ready-to-use, real-world application, the asserted utility is not substantial.

3. *to promote wound healing*. This asserted utility is not specific or substantial. The specification alleges that the IL-20 polypeptide plays a role in wound healing because the (expression level of RNA encoding the cyto10 protein in wounded skin was elevated two fold compared to that of the control sample and therefore the cyto10 protein can be applied to a wound or a burn to promote wound healing see page 34, lines 11-18; Example 4, pages 37-39). However, the specification does not disclose the role of cyto10 protein in wound healing or the result of applying cyto10 to a wound or a burn to promote wound healing. Since the asserted utility is not presented in a ready-to-use, real-world application, the asserted utility is not substantial.

4. *to increase platelet count*. This asserted utility is not specific or substantial.
The experimental evidence presented in Example 8, page 41-42 and page 34, lines 14-19, of the specification is, neither convincing nor specific. The specification asserts that cyto10 affects haematopoiesis and increases platelet counts in both male and female mice treated with Zcyto10-

adenovirus compared to empty adenovirus control but decreases hematocrit and decreases spleen and liver weight in male mice. The specification and does not provide any evidence of cyto10 induced platelet increase. Therefore, since the asserted utility is not presented in a ready-to-use, real-world application, the asserted utility is not substantial.

5. *in the treatment of disease.* The asserted utility is not specific or substantial.

The specification on page 31, lines 21-36 and page 32, lines 1-4, discloses that

"Zcyto10 polypeptides, agonists or antagonists thereof may be therapeutically useful in the regeneration of the gastrointestinal tract or oral cavity.

Zcyto10 polypeptides, agonists or antagonists thereof may be useful in the treatment of asthma and other diseases of the tracheobronchial tract, such as bronchitis and the like, by intervention in the cross-regulation of Th1 and Th2 lymphocytes, regulation of growth, differentiation and cytokine production of other inflammatory cellular mediators, such as eosinophils, mast cells, basophils, neutrophils and macrophages. Zcyto10 polypeptides, agonists or antagonists thereof may also modulate muscle tone in the tracheobronchial tract. Zcyto10 polypeptides can also be used to treat a number of skin conditions either systemically or locally when placed in an ointment or cream, for example eczema, psoriasis or dry skin conditions in general or as related skin attentions. Also the Zcyto10 polypeptide can be directly injected into muscle to treat muscle atrophy in the elderly, the sick or the bed-ridden.

The specification does not disclose any specific diseases or disorders associated with human cyto10. Since the asserted utility of using the IL-20 polypeptide as a therapeutic is not presented in a ready-to-use, real-world. application, the asserted utility is not substantial.

Claim rejections-35 USC § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The instant specification does not disclose a biological activity for the claimed polynucleotide encoding the Zcyto7protein, therefore, there is no specific and substantial asserted utility or well established for the claimed polynucleotide encoding the Zcyto7 protein.

Claim rejections-35 USC § 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 19-21, 32-34, 37, 41-43 and 46 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art

clearly would not know how to use the claimed invention. The instant specification does not disclose a biological activity for the claimed polynucleotide encoding the Zcyto7protein, therefore, there is no specific and substantial asserted utility or well established for the claimed polynucleotide encoding the Zcyto7 protein.

Claim rejections-35 USC § 112, first paragraph, written description

6. Claims 1-3, 32, 41, are rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an expression vector comprising a DNA encoding a polypeptide having at least 90% amino acid sequence identity with a particular disclosed sequence (SEQ ID NO:2). The claims do not require that the polypeptide encoded by the claimed polynucleotide possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides encoding polypeptides that is defined only by sequence identity. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of

any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics and structure/function relationship, the specification does not provide adequate written description of the claimed genus.

Vas-cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the ad that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the written description' inquiry, whatever is *now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a nucleic acid encoding a polypeptide of amino acid sequence set forth in SEQ ID NO:2, but not the full breadth of the claims meets the written description provision of 35

U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim rejections-35 USC § 112, first paragraph, scope of enablement

7. Claims 1-3, 32, 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide of amino acid sequence set forth in SEQ ID NO:2, does not reasonably provide enablement for an isolated polynucleotide encoding a polypeptide having at least 90% amino acid sequence identity with a particular disclosed sequence (SEQ ID NO:2). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 1, for example, is overly broad in its limitation of "at least 90% identical" because no guidance is provided as to which of the myriad of nucleic acid molecules encompassed by the claims will encode a polypeptide with the desired property. Variants of a nucleic acid can be generated by deletions, insertions, and substitutions of nucleotides, but no actual or prophetic examples on expected performance parameters of any of the possible variants of the claimed nucleic acid molecule or muteins of the protein molecule have been disclosed. Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet,

despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate and use a nucleic acid encoding a polypeptide having at least 90% amino acid sequence identity with SEQ ID NO:2 other than the polypeptide of SEQ ID NO:2 exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of the claims, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim rejections-Double Patenting

Non-statutory double patenting rejection (obviousness-type)

8. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and 8 may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8a. Claims 1-2, 4-5, 7-8, 19-20, 32-34, 37, 41-43, 46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8, of copending Application No. 10/789,129. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-4, 8 of (having all common inventors with the instant application), claims a polynucleotide encoding a polypeptide of amino acid sequence set forth in SEQ ID NO:2 or a polynucleotide encoding a polypeptide that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:2. Claim 1, for example, in application 10/789,129, is generic to claim 1 in the instant application and encompasses subject matter to which the claims in the instant application are a species because a polynucleotide encoding a polypeptide of amino acid sequence 90% identical to the amino acid sequence set forth in SEQ ID NO:2 includes an expression vector comprising a polynucleotide encoding a polypeptide of amino acid sequence 90% identical to the amino acid sequence set forth in SEQ ID NO:2. However, the instant claims are obvious from the claims in 10/789,129 because the instant claims are directed to specific embodiments encompassed by the claims in 10/789,129. Furthermore, in 10/789,129 there are no claims drawn to a host cell comprising the polynucleotide and a method of producing the polypeptide. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant invention was made to place the polynucleotide encoding the IL-20 polypeptide, in an expression vector and host cell which expresses the putative protein encoded thereby, and recovering the recombinant protein produced. To have incorporated the recombinant polynucleotide encoding the IL-20 protein into an expression vector and host cell to facilitate the production and characterization of the IL-20 protein encoded thereby by employing those methods that were old and well known in the art of

molecular biology at the time that the instant invention was made would have been *prima facie* obvious to an artisan in light of the 10/789,129 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8b. Claims 3, 6, 9, 21, are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8 of copending Application No. 10/789,129 in view of Capon et al. (U.S. Patent No. 5,116,964).

This is a provisional obviousness-type double patenting rejection.

Claim 3, for example, in the instant application claims "an expression vector comprising a polynucleotide encoding a polypeptide of amino acid sequence 90% identical to the amino acid sequence set forth in SEQ ID NO:2, wherein the polypeptide comprises an immunoglobulin constant region. Claim 1, for example, of application 10/789,129 (having all common inventors with the instant application), claims "a polynucleotide encoding a polypeptide that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:2". It is clear that the claims differ in scope because claim 3 of the instant application recites "comprises an immunoglobulin constant region". Therefore, claim 1 in 10/789,129 is generic to claim 3 in the instant application and encompasses subject matter to which claim 3 in the instant application is a species. The instant claims are obvious from the claims in 10/789,129 because the instant claims are directed to specific embodiments encompassed by claims 10/789,129. The instant products are included in the 10/789,129 claims. Similarly, instant claims 6, 9, and 21, are species claims of claims 1-4 and 8 on 10/789,129. However, the product claims in 10/789,129 fail to teach the

immunoglobulin constant region to which the IL-20 polypeptide is bonded to increase the half-life of IL-20.

Capon et al. teaches chimeric proteins for directing ligand binding partners such as growth factors, hormones or effector molecules to cells bearing ligands for the ligand binding partners comprising a ligand binding partner fused to a stable plasma protein which is capable of extending the in vivo half-life of the ligand binding partner when present as a fusion with the ligand binding partner, in particular wherein such a stable plasma protein is an immunoglobulin constant domain (see column 4, lines 57-64; column 5, lines 11-21; column 7, lines 11-27; column 8, lines 13-15).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art to modify the polynucleotide encoding the IL-20 polypeptide of 10/789,129 such that it includes the IL-20 polypeptide bonded to the immunoglobulin constant region to obtain a chimeric protein with an increased circulating half-life, as taught by Capon et al., to obtain the known functions and advantages of IL-20. One would have been motivated to use a chimeric protein comprising IL-20 and the immunoglobulin constant region to decrease its clearance rate *in vivo*. Therefore, it would have been obvious to fuse IL-20 with the immunoglobulin constant region, a long-lived molecule well known in the art as able to increase the stability of rapidly cleared molecules.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 1-9, 19-21, 32-34, 37, 41-43, 46 are rejected.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
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